

Assessment of Naïve Inhaler User Inhalation Profiles and the Impact on Subsequent Aerosol Performance : Comparison of a Dry Powder Inhaler and a Pressurized Metered Dose Inhaler with Valved Holding Chamber Using the Same Active Pharmaceutical Ingredients

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KEY MESSAGE

- Inhalation breathing patterns have the potential to differ greatly from one individual to another.
- Such variability appears to impact the fine particle mass delivery more so with the Dry Powder Inhaler (DPI) platform than the Pressurized Metered Dose Inhaler (pMDI) with Valved Holding Chamber (VHC).

INTRODUCTION

- The present scoping study examined the potential impact of variable inhalation technique (recorded from 3 adult volunteers) on fine particle mass (FPM<5.0 µm) emitted from the Diskus[†] DPI, compared with the same measure emitted from a pMDI+VHC incorporating the same active pharmaceutical ingredients.
- The volunteers were trained in the use of the DPI by means of on-line video instruction aids and by following the manufacturer's instructions-for-use in the case of inhalation via the pMDI with VHC.

MATERIALS AND METHODS

DPI Inhalation Evaluation

- Advair[†] Diskus[†] DPI (GlaxoSmithKline)
 - 250 µg/actuation Fluticasone Propionate (FP) + 50 µg/actuation Salmeterol Xinafoate (SX)
- Three DPI naïve adult participants were asked to inhale from this open DPI and their inhalation flow rate-elapsed time profiles were recorded

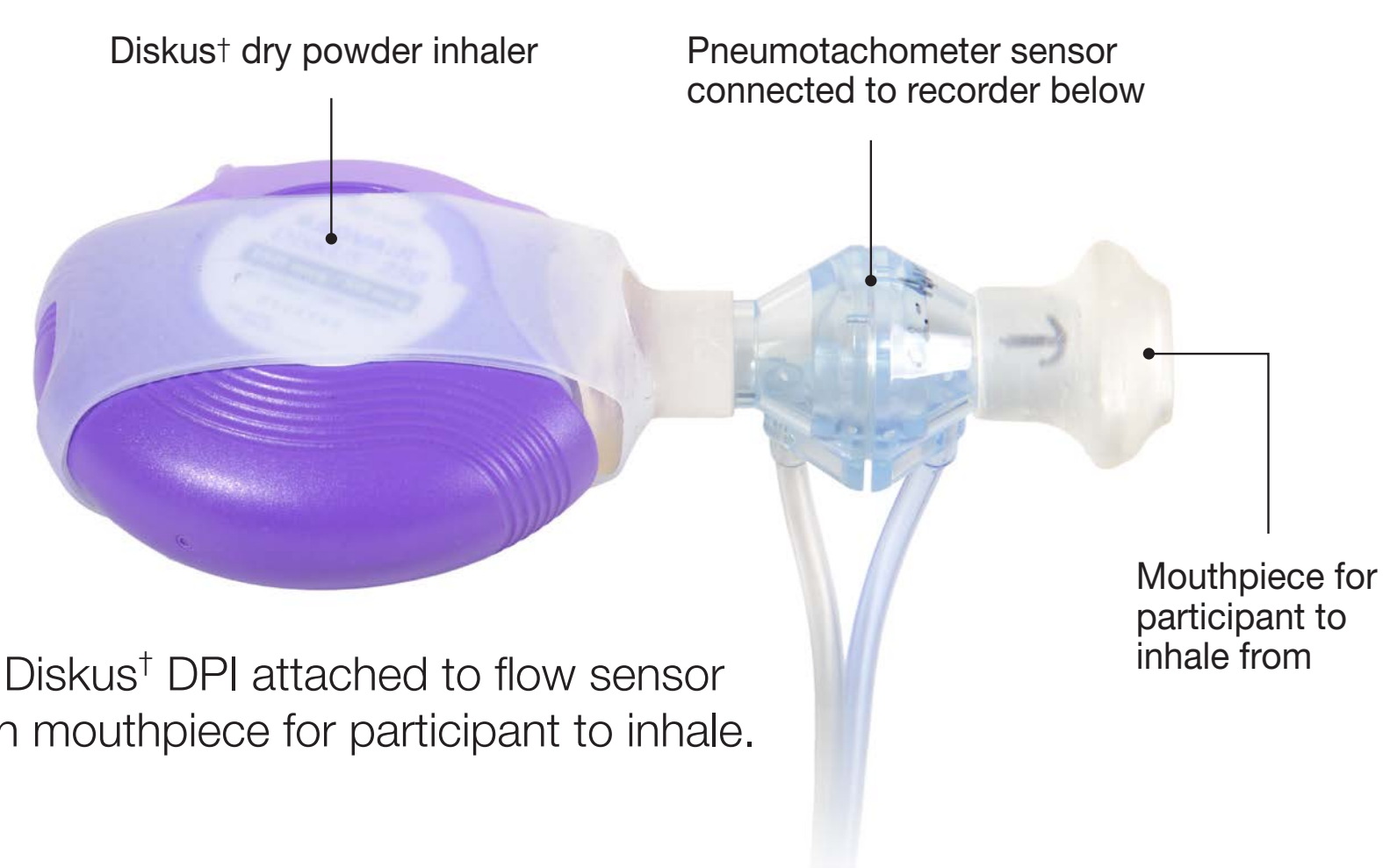


Figure 1: Diskus[†] DPI attached to flow sensor holder with mouthpiece for participant to inhale.

pMDI+VHC Inhalation Evaluation

- Advair[†] Evohaler[†] pMDI (GlaxoSmithKline) connected to AeroChamber Plus[†] Flow-Vu[†] VHC (Trudell Medical International).
 - 250 µg/actuation FP + 25 µg/actuation SX
- The volunteers were each asked to inhale from the mouthpiece of the VHC in two different ways following the manufacturer's instructions
 - Exhale and press the inhaler once at the beginning of a slow inhalation then breathe in and out through the chamber for 2-3 breaths keeping lips sealed around chamber mouthpiece (tidal breathing)
 - Exhale then press the inhaler once at the beginning of a slow inhalation, then inhale slowly and deeply through the VHC until a full breath has been taken (single breath)

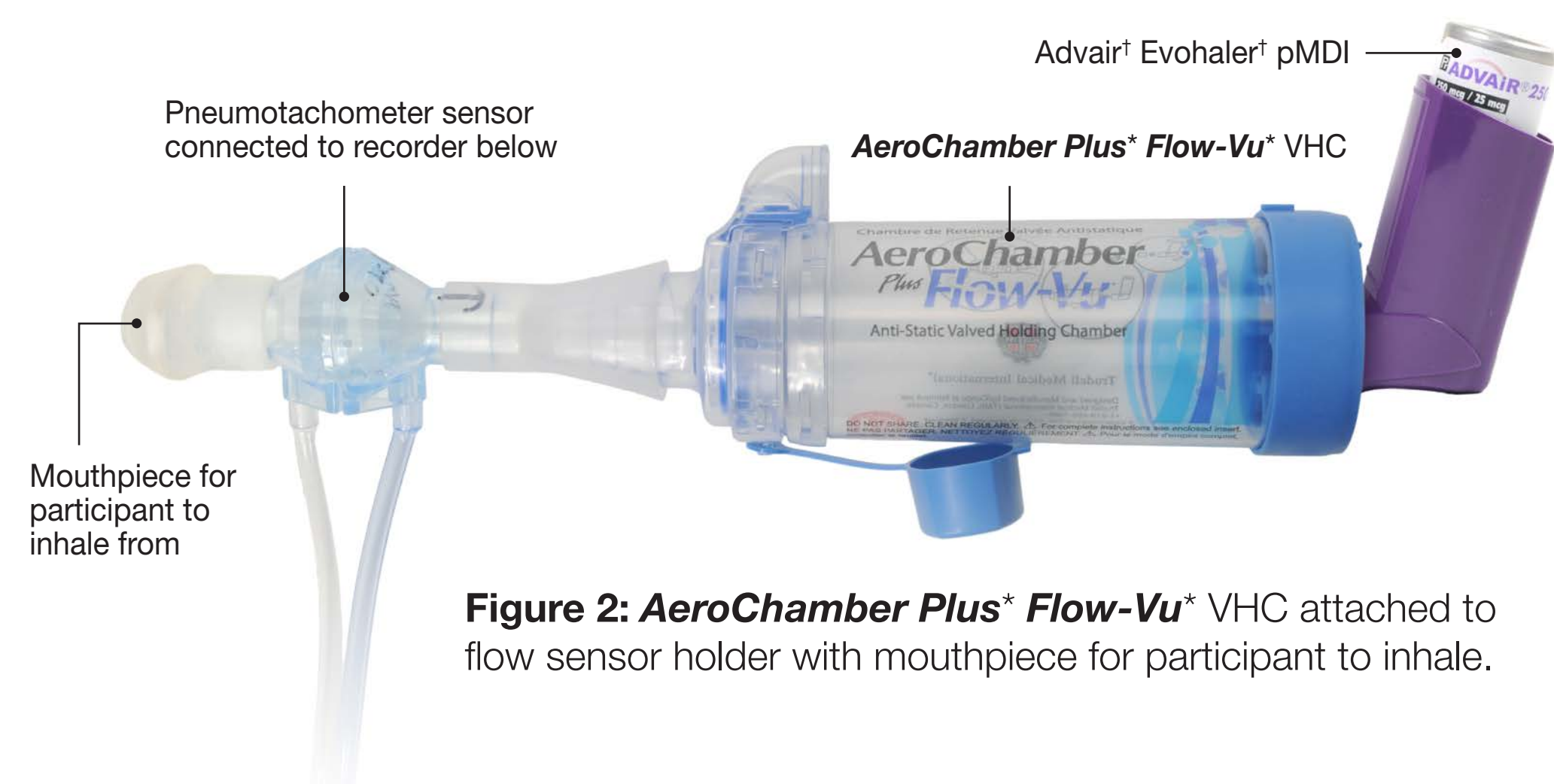


Figure 2: AeroChamber Plus[†] Flow-Vu[†] VHC attached to flow sensor holder with mouthpiece for participant to inhale.

Aerosol Performance

- The inhalation patterns from the participant recorded breathing profiles were subsequently programmed into a breathing simulator
- APSD measurements were then made for both DPI and pMDI+VHC

RESULTS

Breathing Profiles

DPI

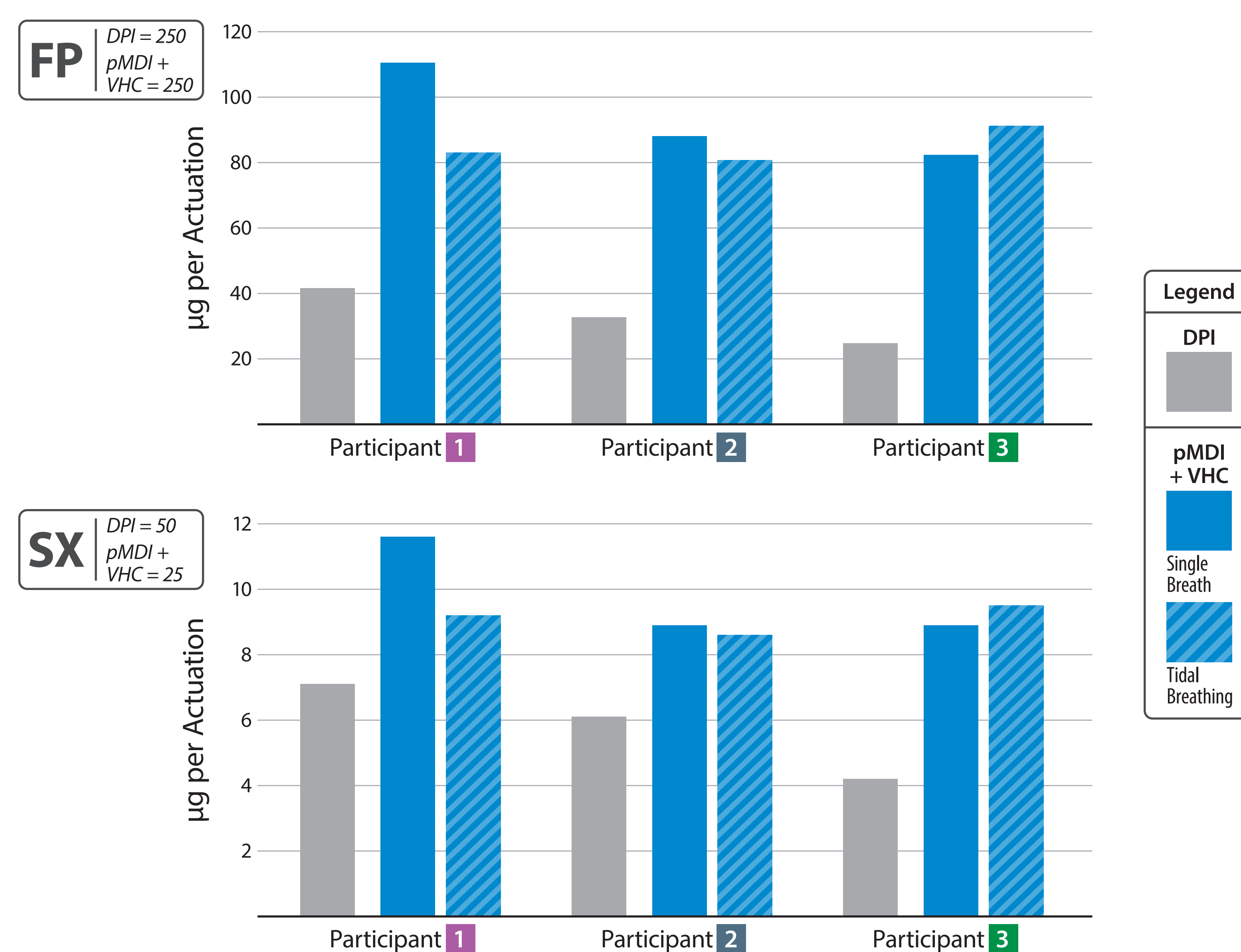
Participant	V _{inspired} (mL)	PIFR (L/min)
1	1876	163.0
2	2099	125.7
3	621	25.7

pMDI + VHC

Participant	Tidal Volume (mL)			Single Breath Volume (mL)
	Breath 1	Breath 2	Breath 3	
1	953	1029	not made	1302
2	968	1165	818	1611
3	198	404	595	350

Aerosol Performance

Fine Particle Mass (<5.0 µm) — DPI vs. pMDI+VHC



DPI

Participant	1		2		3	
	FP	SX	FP	SX	FP	SX
FPF<5.0 µm (%)	21.6	19.3	16.6	15.3	21.9	19.4
FPM<5.0 µm (µg/actuation)	41.6	7.1	32.7	6.1	24.8	4.2

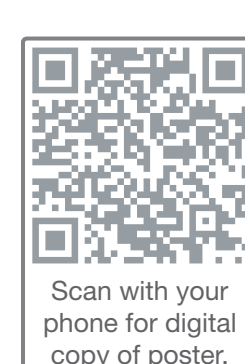
pMDI + VHC

Participant	1		2		3							
	Single Breath		Tidal Breathing		Single Breath		Tidal Breathing					
	FP	SX	FP	SX	FP	SX	FP	SX				
FPF<5.0 µm (%)	93.9	96.0	92.2	92.4	83.6	89.6	83.9	86.2	92.5	93.3	93.3	95.9
FPM<5.0 µm (µg/actuation)	110.5	11.6	83.1	9.2	88.1	8.9	80.7	8.6	82.4	8.9	91.2	9.5

- Interpolation to a common size limit was required because the NGI was operated at the two different flow rates (60 L/min, DPI; 30 L/min, pMDI+VHC) appropriate for the different inhaler classes.
- Associated measures of measurement variance (± S.D.) are not reported because these measures cannot be interpolated. However, all values for each data set were <15%, and most were <10% of the mean value for each data set.

CONCLUSIONS

- The DPI results suggest that inhalation breathing profiles can have an appreciable impact upon aerosol delivery, with one participant having much less predicted medication as fine particles
- In contrast, although the inhalation profiles across all participants were also divergent when asked to inhale from the pMDI + VHC, either tidal breathing or by a slow, deep inhalation, all volunteers would have received a relatively consistent amount of medication.
- It also appears that the pMDI + VHC platform delivers a larger FPM<5.0 µm for both APIs and a consequently smaller coarse particle mass. However, it is recognized that more investigation is warranted with a larger number of volunteers and with other passive DPIs having different resistances.



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